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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/982,531 | 10/19/2001 | Astrid Vrang | 54320.000011 | 8179 |

7590 10/23/2006

Stanislaus Aksman
Hunton & Williams
Suite 1200
1900 K Street, N.W.
Washington, DC 20006

EXAMINER

VOGEL, NANCY S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1636

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|-------------------------------|------------------------------|--|
| Office Action Summary | Application No. 09/982,531 | Applicant(s) VRANG ET AL. | |
| | Examiner Nancy T. Vogel | Art Unit 1636 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 14, 17, 24, 27 and 30-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 14, 17, 24, 27, 30-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-11, 14, 17, 24, 27 and 30-45 are pending in the case.

Any rejection of record in the previous action not addressed in this office action is withdrawn.

The following is a new rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 14, 17, 24, 27, 30-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing heterologous polypeptides or peptides or proteins in *Lactococcus lactis*, does not reasonably provide enablement for methods for producing heterologous polypeptides, peptides or proteins in any lactic acid bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples,

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6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method of producing heterologous proteins in lactic acid bacteria, using chemically defined media and fed-batch or continuous cultivation.

The state of the prior art was advanced, in that methods of cell culture for the production of heterologous proteins was well known, although the field was well developed for use of such well known hosts as *E. coli*, but not for non-traditional recombinant hosts such as lactic acid bacteria.

The relative skill of those of those in the art was moderate, in that in general trial and error is used to determine optimal conditions for obtaining maximal amounts of a recombinant protein during cell culture.

The level of predictability of the art is very high, since it cannot be accurately predicted which growth media and conditions will result in maximal amounts of a recombinant protein in any particular cell type. For example, Jensen et al. (Appl. Environ. Microbiol. 59, 12, p. 4363-4366, 1993) disclosed that one particular lactic acid bacteria, *Lactococcus lactis*, has numerous growth requirements which required a particular combination of amino acids for sufficient growth, and that experimentation was required to determine appropriate conditions (page 4363). There is no expectation that the particular growth conditions needed for *L. lactis* would be appropriate for other types of lactic acid bacteria.

The existence of working examples in the specification is limited, since only methods using *Lactococcus lactis* are used.

The breadth of the claims is large, since the claims are drawn to methods using any lactic acid bacteria, and therefore encompasses all of the types of bacteria which includes such diverse organisms as defined in the specification, as follows:

"*Lactococcus* spp., *Streptococcus* spp., *Lactobacillus* spp., *Leuconostoc* spp., *Pediococcus* spp., *Brevibacterium* spp. and *Propionibacterium* spp. Additionally, lactic acid producing bacteria belonging to the group 30 of the strictly anaerobic bacteria, bifidobacteria, ie *Bifidobacterium* spp., which are frequently used as food starter cultures alone or in combination with lactic acid bacteria, are generally included in the group of lactic acid bacteria" (page 6 of the specification).

The amount of guidance provided by the specification is limited, since the only guidance in the specification is limited to the disclosed method as applied to *Lactococcus lactis*.

Claims 6, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in

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the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 6 and 35 are drawn to methods using a regulatable promoter which is "the P170 promoter disclosed in WO 98/10079 or a derivative thereof". The specification has not defined what is encompassed by the term "derivative" and therefore it is given the broadest reasonable interpretation, and is interpreted to encompass any nucleotide sequence which is a regulatable promoter, since any nucleotide sequence can be derived from another by substitution, addition, or deletion. Claims 6 and 35 are genus claims in terms of a nucleotide sequence which functions as a regulatable promoter, which has an undefined structure or sequence. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all DNA molecules which have regulatable promoter activity in the lactic acid bacteria and which are derived from the P170 promoter. While the specification provides general information on a particular promoter P170 and its structure and function, there is no disclosure of the precise nucleotides therein which could be modified by insertion, substitution or deletion and retain regulatable promoter activity in lactic acid bacteria. Therefore, the specification does not describe the claimed DNA in such full, clear, concise and exact terms so as to indicate that Applicant had possession of the product at the time of filing the present application. Thus the written description requirement has not been satisfied.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 5 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of "derived from a lactic acid bacterium", since "derived" is a term that is non-specific and relative in nature for which Applicant provides no definition. It provides no clarity as to what Applicant's claimed invention includes and what it does not include. Without a more specific definition, it is impossible to determine what and how many derivations comprise the invention. The nature and number of the derivations to arrive at the invention Applicant seeks to protect with the patent are not established such that a person skilled in the art would be apprised of the metes and bounds of the claims. The limits of the inventions cannot be discerned and others could not know if they were infringing Applicant's claim.

The Declaration under 37 CFR 1.132 filed 7/25/06 is sufficient to overcome the rejections of claims 1-11, 14, 17, 24, 30-45 based upon 35 USC 103.

Conclusion

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV
10/11/06


NANCY VOGEL
PRIMARY EXAMINER